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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants : Ann Marie Schmidt and David Stern

Serial No. : 09/166,649

Filed : October 5, 1998 Group Art Unit: 1615

For : METHODS FOR DETERMINING WHETHER A COMPOUND IS CAPABLE OF INHIBITING THE INTERACTION OF A PEPTIDE WITH RAGE

1185 Ave. of the Americas
New York, New York 10036
April 15, 1999

Assistant Commissioner for Patents
Washington, D.C. 20231

Sir:

INFORMATION DISCLOSURE STATEMENT

In accordance with their duty of disclosure under 37 C.F.R. §1.56, applicants would like to direct the Examiner's attention to the following disclosures, which are listed on Form PTO-1449 (Exhibit 1). Copies of the disclosures listed below as items 1-28 are attached hereto as Exhibits 2-29, respectively.

1. Brett, J, et al., (1993) "Survey of the distribution of a newly-characterized receptor for AGEs in tissues" Am. J. Pathol, 143:1699-1712 (Exhibit 2);

2. Fu, M-X., et al. (1996) "The Advanced Glycation Endproduct, N^{e}-(Carboxymethyl)lysine is a product of both lipid peroxidation and glycoxidation reactions" J. Biol. Chem., 271:9982-9986 (Exhibit 3);

3. Khoury, J., et al., (1994) "Macrophages adhere to glucose-modified basement membrane via their scavenger receptors" J. Biol. Chem., 269:10197-10200 (Exhibit 4);

4. Lander, H. L., et al. (1997) "Activation of the Receptor

for Advanced Glycation Endproducts triggers a MAP Kinase pathway regulated by oxidant stress" J. Biol. Chem., 272:17810-17814 (Exhibit 5);

5. Li, J. and Schmidt, A. M. (1997) "Characterization and functional analysis of the promoter of RAGE, the Receptor for Advanced Glycation Endproducts" J. Biol. Chem., 272:16498-16506 (Exhibit 6);

6. Marui, N., et al. (1993) "VCAM-1 gene transcription and expression are regulated through an oxidant-sensitive mechanism in human vascular endothelial cells" J. Clin. Invest., 92:1866-1874 (Exhibit 7);

7. Miyata, T., et al. (1996) "The Receptor for Advanced Glycation Endproducts (RAGE) mediates the interaction of AGE-b^2-Microglobulin with human mononuclear phagocytes via an oxidant-sensitive pathway: implications for the pathogenesis of dialysis-related amyloidosis" J. Clin. Invest., 98:1088-1094 (Exhibit 8);

8. Park, L., et al. (1998) "Suppression of accelerated diabetic atherosclerosis by soluble Receptor for AGE (sRAGE)" Nature Medicine, 4:1025-1031 (Exhibit 9);

9. Portero-Otin, M., et al. (1995) "Chromatographic evidence for pyrraline formation during protein glycation *in vitro* and *in vivo*" Biochim. Biophys. Acta, 1247:74-80 (Exhibit 10);

10. Reddy, S., et al. (1995) "N^e-(Carboxymethyl)lysine is a dominant Advanced Glycation Endproduct (AGE) antigen in tissue proteins" Biochemistry, 34:10872-10878 (Exhibit 11);

11. Schleicher, E. D., et al. (1997) "Increased accumulation of

the glycoxidation product N^e-(Carboxymethyl)lysine in human tissues in diabetes and aging" J. Clin. Invest., 99:457-468 (Exhibit 12);

12. Schmidt, A-M, et al. (1992) "Isolation and characterization of binding proteins for advanced glycation endproducts from lung tissue which are present on the endothelial cell surface" J. Biol. Chem., 267:14987-14997 (Exhibit 13);

13. Schmidt, A. M., et al. (1997) "The V-Domain of Receptor for Advanced Glycation Endproducts (RAGE) mediates binding of AGEs: a novel target for therapy of diabetes" Circulation Supplement, 96:#194, p. I-37 (Exhibit 14);

14. Schmidt, A. M., et al. (1994) "The endothelial cell binding site for advanced glycation endproducts consists of a complex: an integral membrane protein and a lactoferrin-like polypeptide" J. Biol. Chem., 269:9882-9888 (Exhibit 15);

15. Schmidt, A-M, et al. (1994) "Cellular receptors for advanced glycation end products" Arterioscler. Thromb., 14:1521-1528 (Exhibit 16);

16. Schmidt, A. M., et al (1995) "The Dark Side of Glucose (News and Views)" Nature Medicine, 1:1002-1004 (Exhibit 17);

17. Schmidt, A-M, et al. (1993) "Regulation of mononuclear phagocyte migration by cell surface binding proteins for advanced glycosylation endproducts" J. Clin. Invest., 92:2155-2168 (Exhibit 18);

18. Schmidt, A-M, et al. (1994) "Receptor for advanced glycation endproducts (AGEs) has a central role in vessel

wall interactions and gene activation in response to circulating AGE proteins" Proc. Natl. Acad. Sci. (USA), 91:8807-8811 (Exhibit 19);

19. Schmidt, A. M., et al. (1995) "AGE interaction with their endothelial receptor induce expression of VCAM-1: a potential mechanism for the accelerated vasculopathy of diabetes" J. Clin. Invest., 96:1395-1403 (Exhibit 20);

20 Schreiber, E., et al. (1989) "Rapid detection of octamer binding proteins with 'mini-extracts' prepared from a small number of cells" Nucleic Acids Research, 17:6419 (Exhibit 21);

21. Sell, D. R., and Monnier, V. M. (1989) "Structure elucidation of a senescence cross-link from human extracellular matrix" J. Biol. Chem., 264(36): 21597-21602 (Exhibit 22);

22. Shamsi, F. A., et al. (1998) "Immunological evidence for methylglyoxal-derived modifications *in vivo*" J. Biol. Chem., 273:6928-6936 (Exhibit 23);

23. Soulis T., et al. (1997) "Advanced glycation endproducts and their receptors co-localize in rat organs susceptible to diabetic microvascular injury" Diabetologia, 40:619-628 (Exhibit 24);

24. Vlassara, H., et al. (1995) "Identification of Galectin-2 as a high affinity binding protein for Advanced Glycation Endproducts (AGE): a new member of the AGE-Receptor complex" Molecular Medicine, 1:634-646 (Exhibit 25);

25. Wautier, J. L., et al. (1996) "Receptor-mediated endothelial dysfunction in diabetic vasculopathy: sRAGE

blocks hyperpermeability" J. Clin. Invest., 97:238-243 (Exhibit 26);

26. Wu J., et al. (1997) "The soluble receptor for Advanced Glycation Endproducts (sRAGE) ameliorates impaired wound healing in diabetic mice" Plastic Surgery Research Council, Abstract, #77, p. 43 (Exhibit 27);

27. Yan, S-D., et al. (1994) "Enhanced cellular oxidant stress by the interaction of advanced glycation endproducts with their receptors/binding proteins" J. Biol. Chem., 269:9889-9897 (Exhibit 28);

28. Yang, Z., et al (1991) "Two novel rat liver membrane proteins that bind AGEs: relation to macrophage receptor for glucose-modified proteins" J. Exp. Med., 174:515-524 (Exhibit 29);

Applicants request that the Examiner review the references and make them of record in the subject application.

If a telephone interview would be of assistance in advancing prosecution of the subject application, applicants' undersigned attorney invites the Examiner to telephone him at the number provided below.

No fee is deemed necessary in connection with the filing of this Information Disclosure Statement. If any such fee is required, authorization is hereby given to charge the amount of such fee to Deposit Account No. 03-3125.

Respectfully submitted,

I hereby certify that this correspondence is being deposited this date with the U.S. Postal Service with sufficient postage as first class mail in an envelope addressed to: Assistant Commissioner for Patents Washington, D.C. 20231.

4/15/99

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Form PTO-1449	U.S. Department of Commerce Patent and Trademark Office	Atty. Docket No. 0575/56613/JPW/JML	Serial No. 09/166,649
INFORMATION DISCLOSURE STATEMENT (Use several sheets if necessary)		Applicant: Ann Marie Schmidt and David Stern	
		Filing Date: October 5, 1998	Group: 1646

U.S. PATENT DOCUMENTS

Examiner Initial		Document Number	Date	Name	Class	Subclass	Filing Date if Appropriate
		5 8 6 4 0 1 8	1/26/99	Morser et al.			April 16, 1996

FOREIGN PATENT DOCUMENTS

		Document Number	Date	Country	Class	Subclass	Translation	
							Yes	No
	WO	9 7 3 9 1 2 5	10/23/97	PCT				
	WO	9 7 9 2 3 1 1	10/23/97	PCT				
	WO	9 7 2 6 9 1 3	01/21/97	PCT				

OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)

		International Search Report issued for International Application No. PCT/US99/23245, filed 05 October 1999 (**Exhibit D**);
		Mackic, et al. "Human Blood-Brain Barrier for Alzheimer's Amyloid-β 1-40." (J. Clin. Invest., Vol. 102, No. 4, August 1998, pgs. 734-743) (**Exhibit 2**); and
		Bucala et al. "Modification of Low Density Lipoprotein by Advanced Glycation End Products Contributes to the Dyslipidemia of Diabetes and Renal Insufficiency" (Proc. Natl. Acad. Sci. USA., Vol 91, September 1994, pgs. 9441-9445) (**Exhibit 3**).

		EXAMINER	DATE CONSIDERED

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609: Draw line through citation if not in conformance and not considered. Include copy of this from with next communication to applicant.

Applicant: Ann Marie Schmidt and David Stern
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Exhibit E